10-26 are added. Claims 11-26 relate to monoclonal antibody 1A7, and pharmaceutical compositions and kits based thereupon, and therefore fall within elected Group I, presently under examination. Claim 10 relates to the 1A7 producing hybridoma cell line, and falls within elected Group I under the provisions of MPEP § 806.05(c)(2).

The amendments have been made to advance prosection of the subject application, and are not intended to be a dedication to the public of any subject matter of the claims as originally presented.

Specification amendments:

Changes have been made to the specification to correct obvious clerical errors, and thus do not constitute new subject matter.

On page 11, line 20, "Freud's Adjuvant" is a typographical error for "Freund's Adjuvant", which is correctly recited on page 15, line 21; page 15, line 33; and page 16, line 2.

In reference to the assays disclosed on pages 18-19; the context shows that Ab1 or Ab3 were tested at different concentrations. Minor grammatical changes have been made in accordance with the Examiner's suggestions and specification amendments filed previously.

Claim amendments:

The added claims pertain to embodiments of the invention relating to the 1A7 monoclonal antibody, and pharmaceutical compositions and diagnostic kits based thereupon. The added claims therefore fall within Group I, which is presently under examination.

Claims 1, 4, and 7-9 have been amended and reflect that a 1A7 antibody producing cell line is deposited under ATCC Accession No. HB-11786.

Claims 10-12 relate to the 1A7 antibody, antibody preparations, and the cell line deposited under ATCC Accession No. HB-11786. Support for these claims can be found throughout the disclosure, including original claim 1.

Claims 13-19 pertain to pharmaceutical compositions comprising the antibody of the invention, and relate to claim 4. Claim 13 further provides that the antibody of the pharmaceutical composition is capable of binding anti-GD2. 1A7 was demonstrated as capable of binding Ab1 and Ab3 by the data in Figures 1-2. Ab1 and Ab3 were established as anti-GD2 by the data in Figures 3-5.

Claims 14 and 15 further provide that the composition comprise an adjuvant, particularly complete Freund's Adjuvant (page 15, lines 31-33), incomplete Freund's Adjuvant (page 15, line 33 to page 16, line 2); and QS-21 (page 16, lines 7-9). Claim 16 further provides that the composition is for a GD2-associated cancer (page 8, lines 18-22). Claim 17 further provides that the composition is for treatment of the cancers listed on page 8, lines 8-9. Claims 18-19 pertain to pharmaceutical compositions, whereby the monoclonal antibody is

identical to that produced by the cell line deposited with the ATCC (page 10, lines 19-23).

Claims 9 and 20-26 pertain to diagnostic kits. Claims 9 and 20 pertain to diagnostic kits comprising the 1A7 antibody (page 20, line 29 ff). Claims 21-23 further provide that the primary antibody or a second antibody in the kit be provided with a detectable label (page 21, lines 1-16). Claims 24-25 depend from claim 18, and further reflect the objective of detecting melanoma and small cell carcinoma (page 8, lines 8-9). Claim 26 further provides that the sample being tested be obtained from an individual previously treated with the 1A7 antibody, as described in the specification (page 15, line 15 to page 16, line 5).

The added claims have support in the application as filed, and do not constitute new matter.

Objections and Rejections under 35 USC § 112 ¶ 1:

The specification is objected to, and all elected claims are rejected under 35 USC § 112 ¶ 1, for failing to provide an enabling disclosure commensurate in scope with the claimed subject matter. All points were addressed in the amendment filed on November 8, 1995. The following additional remarks are made with respect to some of the points raised.

The identity and source of 14G2a:

The practitioner will readily appreciate that the IgG2ak anti-GD2 mentioned in lines 22-24 as being "used to generate" the Ab2 is the same 14G2a mentioned earlier in the

page. The paragraph beginning on-line 22 is clearly an elaboration of the raising of 1A7 using 14G2a, referred to in lines 7-9. The following paragraph (lines 29 ff) continues: "Several Ab2 hybridomas were obtained that reacted with the *immunizing* Id of 14G2a (Ab1) ..." (emphasis added). 14G2a is the only immunogen described in the specification as being used to raise 1A7, and a practitioner of ordinary skill reading the disclosure is unlikely to be misled on this point.

As agreed at the interview, the 14G2a antibody is not required to make or practice the claimed invention. Applicants acknowledge withdrawal of the requirement for deposit of the 14G2a antibody.

With regards to Claim 9:

The Examiner asserts that the specification fails to enable the diagnostic test kit of claim 9, which is herein amended. Added claims 20-26 also pertain to diagnostic test kits.

As disclosed in the specification, the 1A7 monoclonal antibody (Ab2) may be used in plate-binding assays to detect both Ab1 and Ab3 anti-GD2 (Figures 1-2). The 1A7 may be either attached directly to the plate as a capture antibody (Figure 1) or used in fluid phase (Figure 2). Anti-GD2 may arise spontaneously in subjects afflicted with melanoma or small cell carcinoma. Anti-GD2 will also be induced in individuals administered with 1A7, according to this invention (page 15, line 15 ff). The ordinary practitioner will readily appreciate the use of a test kit comprising 1A7 antibody to monitor the

Ab3 response in a subject treated with 1A7, so that the treatment can be continued or modified appropriately.

The Examiner objects to the specification because sera proteins may interfere in these assays. The Examiner cites some of the difficulties of developing hybridoma clones for a diagnostic test. The difficulties described are instability of the cell line, low yield, and failure as a detecting or capture antibody (see Table, page 10 col. 2 of the reference).

This objection is respectfully traversed. The difficulties cited by the Examiner are raised by Seaver with respect to the *development of new hybridoma clones, starting with a new antigen.* None of the difficulties listed in the Table apply to 1A7. As described in the specification, 1A7 has been perpetuated in culture and used to prepare sufficient purified antibody, not only to conduct radioimmunoassays, but also for administration of 2 mg doses. 1A7 was used as both a detecting and a capture antibody in the assay described in Figure 1. Furthermore, the competition experiments outlined in Figure 2 indicate that 1A7 has the sensitivity, specificity, and affinity necessary for a reliable diagnostic assay.

There is no reason to expect that serum proteins would interfere in any such assay. In fact, as disclosed in the specification, diagnostic assays *have been conducted with real clinical specimens.* In the immunization experiments (e.g., page 15, line 30 to page 16, line 5), the presence of Ab3 was detected in the *sera* of immunized animals using Ab2, i.e. 1A7. The ELISA used under such conditions is described in detail on page 17, lines 9-18.

The Examiner further objects to the specification

because there was no demonstration that assay data correlates with the detection of melanoma and small cell carcinoma. This objection presumably stems from recitation in claim 9 of a diagnostic test kit "for the detection of melanoma" and other cancers.

The specificity of monoclonal antibody 1A7 is for the anti-GD2 antibody 14G2a. Accordingly, 1A7 can be used to detect or quantify the presence of anti-GD2 antibody similar to 14G2a, whenever such measurement is desired.

It is known in the art that increased expression of tumor-associated antigens in cancer can lead spontaneously to a low-grade immune response against it. In the case of melanoma and small cell carcinoma, such a response may include anti-GD2. Thus, for example, if an assay using 1A7 in a kit was conducted on a clinical sample from an individual with no previous exposure to 1A7, and anti-GD2 antibody was detected, then the presence of a GD2-associated cancer like melanoma would be indicated. This application is encompassed in the original wording of claim 9.

Another application of 1A7 in a kit is to monitor the anti-GD2 antibody response in an individual being treated with 1A7. This is supported, as indicated earlier, by page 15, line 15 to page 16, line 5 of the specification.

To capture these applications generically, claim 9 has been amended to refer to a kit comprising 1A7 for the detection of anti-GD2 antibody. Dependent claims 24 and 25 refer to the application where an individual is suspected of having a GD2 associated cancer. Dependent claim 26 refer to the application where an individual has been treated with 1A7.

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Applicants request that all objections and rejections be reconsidered and withdrawn. Applicants further submit that newly added claims 10-26 are patentable over inventions previously in the possession of the public. Applicants respectfully request allowance of all pending claims currently under examination.

Respectfully submitted,
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